PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Shogo ISHIUCHI

Appln. No.: 10/509,379

Confirmation No.: 5052

Filed: September 27, 2004

For: REMEDY FOR GLIOBLASTOMA

Docket No: Q83588

Group Art Unit: 1615

Examiner: Snigdha MAEWALL

SUBMISSION OF EXECUTED DECLARATION UNDER 37 C.F.R. §1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Submitted herewith is a copy of an executed Declaration Under 37 C.F.R. §1.132 signed by Shogo ISHIUCHI on March 12, 2009. Consideration and entry of the Declaration are respectfully requested.

Respectfully submitted,

/Sunhee Lee/

Sunhee Lee
Registration No. 53,892

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON DC SUGHRUE/265550

65565
CUSTOMER NUMBER

Date: March 20, 2009

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Shogo ISHIUCHI

Appln. No.: 10/509,379

Confirmation No.: 5052

Filed: September 27, 2004

For: REMEDY FOR GLIOBLASTOMA

Docket No: Q83588

Group Art Unit: 1615

Examiner: Snigdha MAEWALL

DECLARATION UNDER 37 C.F.R. § 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Shogo ISHIUCHI, hereby declare and state:

THAT I am a citizen of JAPAN;

THAT I have received the degree of M.D. in 1998 from Gunma University; and

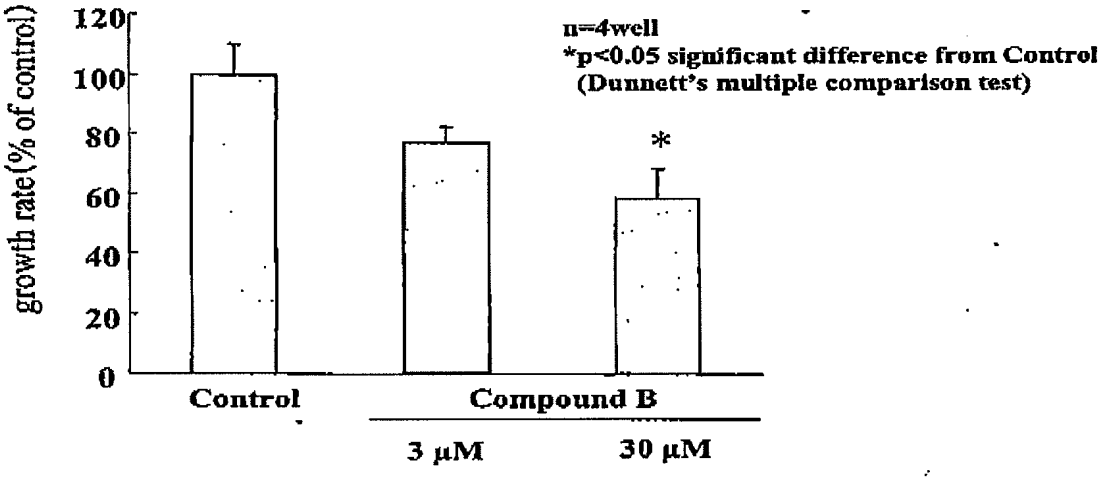
THAT I have been employed by Department of Nuerosurgery, Gunma University School of Medicine since 1999, where I hold a position as Associate Professor, with responsibility for Medical Director.

I further declare that I am the inventor of the above-identified application and familiar with the Office Action mailed November 21, 2008. In the Office Action, the Office asserts that claims 13-16 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for "7-acetyl-5-(4-aminophenyl)-8(R)-methyl-8,9-dihydro-7H-1,3-dioxolo [4,5-h][2,3]benzodiazepine (Talampanel) in treating gliobalstoma, does not reasonably provide enablement for each and every compound claimed. Paragraph 4 on page 5 of the Office Action.

Test 1 Inhibitory effects of compound B on glioblastoma growth -in vitro-

Human glioblastoma cell (CGNH-89 cell line) was used at this experiment. The cells were inocubated at 1 x 10^5 cells per well into well plates containing Eagle's medium with 5% serum. These cells were randomly divided in the following three groups 1 day after seeding: control group, 3μM compound B applied group and 30μM compound B applied group. The cells were incubated for 96 hours. The CGNH-89 cell was cultured in DMEM (Dulbecco's modified Eagle's medium) with glutamine-free and glutamate-free. Each group was set at 4 wells.
The anti-tumor action was evaluated by determining cell count per well using a hemocytometer 96 hours after culturing.
The results are shown as mean ± standard error and statistically analyzed by the Dunnett's multiple comparison test. Significance level was set at $p<0.05$.
As shown in Figure 1, compound B inhibited dose-dependently the growth of CGNH-89 cells with 42.1% inhibition at 30μM.

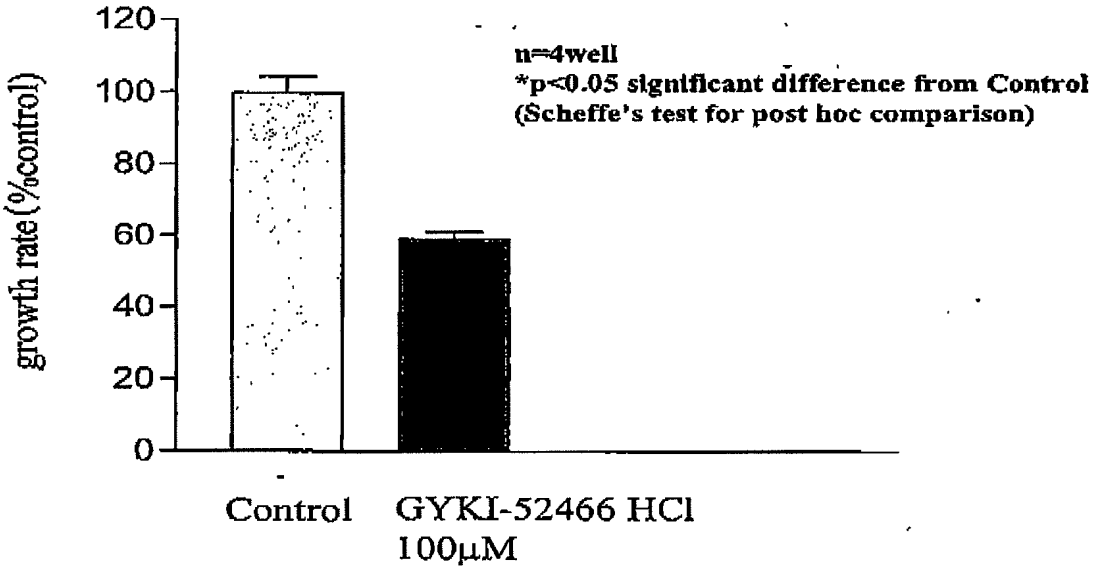
Figure 1



Test 2 Inhibitory effects of GYKI52466 HCl salt on glioblastoma growth -in vitro-

Human glioblastoma cell (CGNH-89 cell line) was used at this experiment. The cells were inocubated at 1 x 10^5 cells per well into well plates containing Eagle's medium with 5% serum. These cells were randomly divided in the following two groups 1 day after seeding: control group and 100μM GYKI52466 HCl salt applied group. The cells were incubated for 96 hours. The CGNH-89 cell was cultured in DMEM (Dulbecco's modified Eagle's medium) with glutamine-free and glutamate-free. Each group was set at 4 wells.
The anti-tumor action was evaluated by determining cell count per well using a hemocytometer 96 hours after culturing.
The results are shown as mean ± standard error and statistically analyzed by the Scheffe's test for past hoc comparison . Significance level was set at $p<0.05$.
As shown in Figure 2, GYKI52466 HCl salt inhibited the growth of CGNH-89 cells with 41% inhibition at 100μM ($p<0.001$).

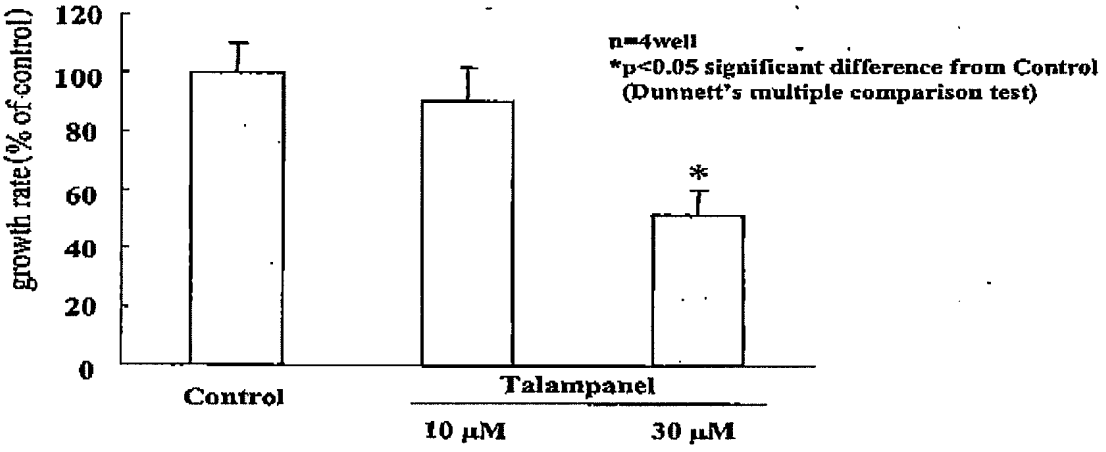
Figure 2



Test 3 Inhibitory effects of Talampanel on glioblastoma growth -in vitro-

Human glioblastoma cell (CGNH-89 cell line) was used at this experiment. The cells were inocubated at 1 x 10^5 cells per well into well plates containing Eagle's medium with 5% serum. These cells were randomly divided in the following three groups 1 day after seeding: control group, 10μM Talampanel applied group and 30μM Talampanel applied group. The cells were incubated for 96 hours. The CGNH-89 cell was cultured in DMEM (Dulbecco's modified Eagle's medium) with glutamine-free and glutamate-free. Each group was set at 4 wells.
The anti-tumor action was evaluated by determining cell count per well using a hemocytometer 96 hours after culturing.
The results are shown as mean ± standard error and statistically analyzed by the Dunnett's multiple comparison test. Significance level was set at $p<0.05$.
As shown in Figure 3, Talampanel inhibited dose-dependently the growth of CGNH-89 cells with 48.7% inhibition at 30μM.

Figure 3



I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: March 12, 2009

S. Ishiuchi
Shogo ISHIUCHI